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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,399	02/17/2004	Galla Chandra Rao	IMMC 308 PCT/US	1615

40541 7590 06/15/2007

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
06/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,399	RAO ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of claims 44-61, without traverse, filed on March 21, 2007, is acknowledged and has been entered. Claims 1-43 have been cancelled. Currently, claims 44-61 are pending and are under examination.

Specification

2. The disclosure is objected to because of the following informalities: In page 16, line 30 of the specification, "referes" should be "refers". Please correct any other spelling errors that may be found in the specification.

Appropriate correction is required.

Trademark Usage

3. The use of the trademark "CellSpotter", "CellTracks", "CellQuest" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 44-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44, step b) is ambiguous in reciting, "preparing a magnetically-labeled sample" because it is unclear how magnetic particles are "sample labels". It is further confusing because the magnetic particles are coupled to a first biospecific ligand which reacts specifically with malignant cells" in the biological specimen comprising mixed cell populations, with the substantial exclusion of other specimen components. Therefore, it appears that it is only the malignant cells that are being magnetically labeled and not the whole sample. See also the recitation of "contacting said magnetically-labeled sample" in step c).

Claim 44, step c) is indefinite in reciting, "contacting ... with at least one additional biospecific ligand which specifically labels said intact malignant cells" because it is unclear how the biospecific ligand specifically labels the intact malignant cells absent recitation of a label conjugated thereto, that is capable of producing a detectable signal.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Specifically, claim 44, step d) is incomplete in reciting, "the presence of said labeled malignant cells ... indicating the presence of

malignancy" because the preamble appears to recite, "A method of monitoring malignancy" which appears to require that the method intends encompassing more than one analysis measured with time interval as a factor; hence, a correlation step appears to be missing. At best, step d) appears to only set forth "A method of determining the presence of malignancy."

Claim 53, step b) is ambiguous in reciting, "preparing a magnetically-labeled sample" because it is unclear how magnetic particles are "sample labels". It is further confusing because the magnetic particles are coupled to a first biospecific ligand which reacts specifically with malignant cells" in the biological specimen comprising mixed cell populations, with the substantial exclusion of other specimen components. Therefore, it appears that it is only the malignant cells that are being magnetically labeled and not the whole sample. See also the recitation of "contacting said magnetically-labeled sample" in step c).

Claim 53, step c) is indefinite in reciting, "contacting ... with at least one additional biospecific ligand which specifically labels said intact malignant cells" because it is unclear how the biospecific ligand specifically labels the intact malignant cells absent recitation of a label conjugated thereto, that is capable of producing a detectable signal.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Specifically, claim 53, step d) is incomplete in reciting, "the presence of said labeled malignant cells ... indicating the presence of

malignancy" because the preamble appears to recite, "A method of monitoring malignancy" which appears to require that the method intends encompassing more than one analysis measured with time interval as a factor; hence, a correlation step appears to be missing. At best, step d) appears to only set forth "A method of determining the presence of malignancy."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 44-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Schmitz et al. (US Patent 6,190,870).

Schmitz et al. disclose an efficient enrichment and detection method and kit for detecting disseminated malignant cells in peripheral blood sample comprising a mixed cell population suspected of containing malignant cells (see Abstract, column 1, lines 33-46, column 2, lines 1-21, and column 9, lines 43-59). The cells are distant from their site of primary tumor, and their presence amongst hematopoietic blood cells is indicative of malignancy (metastatic potential) of the tumor or carcinoma cells (see column 1, lines 35-38). The blood sample is treated with stabilizing agent (fixative) prior

to performing the enrichment method (see column 1, lines 38-40, and column 6, line 44 to column 7, line 4). In practice, the blood sample is mixed with colloidal magnetic particles having specific antibodies coated thereto, that specifically bind a first determinant, i.e. cytokeratin, present in malignant cells (see column 5, lines 29-41, column 7, lines 5-22, and column 8, lines 11-14). The malignant cells comprise cell surface antigens or determinants which are separation markers upon which the antibody-coated magnetic particles specifically bind or react to (see column 2, lines 33-60). The coated magnetic particles are nanoparticles comprising of a core material (magnetic iron-dextran), protein base polymeric coating (biotin, avidin), and antibody that binds to a characteristic determinant of a malignant cell. The size of the magnetic particles are within the range of 10 nm to 100 nm (see column 5, lines 42-67). The sample having magnetically labeled malignant cells are subjected to high gradient magnetic field to produce separated and enriched malignant cell populations (see column 5, lines 15-19 and lines 49-52, and column 7, lines 23-64). The cell mixture is further contacted with specific antibodies conjugated to a detectable label that specifically bind a second determinant present in malignant cells. Reagent labels may include a specific agent capable of labeling non-target entities (blocking agent that reduce non-specific labeling). The detectable labels may comprise a panel (cocktail) of antibodies specific for different malignant cell determinants (see column 6, lines 10-35). Thereafter, the antibody-coated magnetic particle – malignant cell – antibody label complexes are analyzed for the presence of labeled malignant cells, the presence of which provides indication of the presence of malignancy. Analysis of the presence of

malignant cells complexed with magnetic particles and detectable labels are performed using flow cytometry, manual cell microscopic analysis, and fluorescent immunocytochemistry microscopic analysis (see column 6, lines 36-43). See also Examples 1-3. The malignant cells may further be characterized as to their phenotype using PCR, ELISA, FISH, chromosome painting, and immunocytochemistry (see column 9, lines 4-15).

In as far as cell fragments, cell debris, and cell clusters amongst malignant cells, it appears that so long as the conserved determinants or cell surface epitopes are present and maintained in the fragments, debris, or clusters in the cell sample along with the malignant cells, for binding to antibody-coated magnetic particles and antibody-conjugated detectable labels that are specific for the desired conserved epitope common to all intact malignant cells, cell fragments, cell debris, and cell clusters, it would appear that all of the intact malignant cells, cell fragments, cell debris, and malignant cell clusters will be detected and analyzed as to their presence and characterization to provide indication of the presence of malignancy in a cell sample.

In as far as claims 50-52, Schmitz et al. provide phenotypic characterization of the malignant cells according to fragment length polymorphisms and presence or absence of specific sequences using PCR, ELISA, FISH, and immunocytochemistry (see column 9, lines 4-43).

6. Claims 44-46, 48, 49, 53-55, and 57-61 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodstad et al. (US Patent 6,265,229).

Fodstad et al. disclose an enrichment and detection method and kit for detecting disseminated malignant cells in peripheral blood sample comprising a mixed cell population suspected of containing malignant cells. The staging of disease with regards to whether it is localized or metastatic spread has occurred to other tissues, is of utmost important (see Abstract, column 4, lines 12-19, and column 9, line 57 to column 10, line 22). In practice, the blood sample is mixed with paramagnetic particles having specific antibodies coated thereto, that specifically bind a first determinant (cell surface antigen) present in malignant cells. The sample having magnetically labeled malignant cells are subjected to high gradient magnetic field to produce separated and enriched malignant cell populations (see column 5, line 57 to column 6, line 54). The blood sample may be treated with stabilizing agent (fixative) prior to or after performing the enrichment method. The malignant cells comprise cell surface antigens or determinants upon which the antibody-coated magnetic particles specifically bind or react to (see column 5, lines 13-37). The cell mixture is further contacted with specific antibodies conjugated with a detectable label that specifically bind a second determinant present in malignant cells (see column 8, lines 14-26). The antibody-coated magnetic particle – malignant cell – antibody label complexes are analyzed for the presence of labeled malignant cells, the presence of which provides indication of the presence of malignancy. Analysis of the presence of malignant cells complexed with magnetic particles and detectable labels are performed using microscopic analysis, PCR, and immunocytochemistry (see claims 1, 9-13, and 20).

In as far as cell fragments, cell debris, and cell clusters amongst malignant cells, it appears that so long as the conserved determinants or cell surface epitopes are present and maintained in the fragments, debris, or clusters in the cell sample along with the malignant cells, for binding to monoclonal antibody-coated magnetic particles and antibody-conjugated detectable label that are specific for the desired conserved epitope common to all intact malignant cells, cell fragments, cell debris, and cell clusters, it would appear that all of the intact malignant cells, cell fragments, cell debris, and malignant cell clusters will be detected and analyzed as to their presence and characterization to provide indication of the presence of malignancy in a cell sample.

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gailene R. Gabel
Primary Examiner
Art Unit 1641

June 8, 2007